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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/433,777 | 11/03/1999 | JOEL R. HAYNES | APF-18.20 | 2990 |

22428 7590 03/23/2006

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| EXAMINER | |
|---|---|
| WEHBE, ANNE MARIE SABRINA | |
| **ART UNIT** | **PAPER NUMBER** |
| 1633 | |

DATE MAILED: 03/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/433,777 | HAYNES ET AL. | |
| | Examiner | Art Unit | |
| | Anne Marie S. Wehbe | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12/16/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *48-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *48-77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply*.

## DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed on 12/16/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. As requested, the amendment and response originally filed on 8/10/05 and previously non-entered, see the Advisory Action mailed to applicants on 9/21/05, has been entered. Claims 1-47 are now canceled, and new claims 48-77 have been added. Claims 48-77 are therefore currently pending and under examination in the instant application. An action on the merits follows. Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

It is again noted that although applicant's have elected the species of "lipid adjuvants" for examination in the instant application, the pending claims are not limited to the elected subject matter and continue to read on any adjuvant in a form other than DNA.

### *Claim Rejections - 35 USC § 112*

The rejection of previously pending claims 1, 16, and 33-47 under 35 U.S.C. 112, first paragraph, for lack of enablement is withdrawn over canceled claims 1, 16, and 33-47.

It is noted that the previous grounds of rejection concerning the use of "immune shift" adjuvants has not been applied to new claims 48-77 because the new claims, particularly claims

57 and 73, now recite that the adjuvant is "effective to enhance the T helper 1 (Th1) component of an immune response elicited against the antigen". The working examples in the specification demonstrate that while co-administration of an adjuvant such as MPL cannot shift an immune response to an antigen from Th2 to Th1, working example 1 does show that the Th1 component of an immune response can be increased by the addition of an adjuvant such as MPL.

Applicant's amendment has resulted in the following new grounds of rejection under 35 U.S.C. 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claim 48 lacks antecedent basis for "said composition" recited in line 5. The claim as written is directed to "Coated particles", not a composition. Claims 49-59 depend on claim 48 and thus are included in this rejection.

Claim 54 is further indefinite in that it depends on claim 48, and recites that "the adjuvant is present in the composition in the form of a lipid". However, as claim 48 does not recite a composition, the metes and bounds of this dependent claim cannot be determined. Claim 55 depends on claim 54 and is included in this rejection.

Independent claim 60 lacks antecedent basis for "said composition" recited in line 5. The claim as written is directed to co-administering a nucleic acid and an adjuvant, not a composition. Claims 61-77 depend on claim 60 and thus are included in this rejection.

Claim 70 is further indefinite in that it depends on claim 60, and recites that "the adjuvant is present in the composition in the form of a lipid". However, as claim 60 does not recite a composition, the metes and bounds of this dependent claim cannot be determined. Claim 71 depends on claim 70 and is included in this rejection.

Claim 73 lacks antecedent basis for "said particles". Claim 60, from which claim 73 depends does not recite this limitation.

Claim 74 lacks antecedent basis for "said core carrier particles". Claim 60, from which claim 74 depends, does not recite this limitation.

Claim 75 lacks antecedent basis for "the gold particles". Claim 60, from which claim 75 depends, does not recite this limitation.

***Claim Rejections - 35 USC § 102***

The rejection of previously pending claims 1-2, 7, 12, 15, 27-29, 33, 35, 37, 39, 41, 43, and 46-47 under 35 U.S.C. 102 (e) as being anticipated by U.S. Patent No. 5,925,362, hereafter referred to as Spitler et al., is withdrawn over canceled claims 1-2, 7, 12, 15, 27-29, 33, 35, 37, 39, 41, 43, and 46-47, and **maintained over new claims 60-62, 65, and 69-73**. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that the instant grounds of rejection should not be applied to the new claims because Spitler does not teach co-administration of a nucleic acid encoding and antigen and a lipid adjuvant where the adjuvant is delivered directly into cells.

In response, as discussed in the previous office action, Claim 1 of the Spitler patent recites a method of eliciting an antitumor immune response to prostate tumors in a subject comprising administering to said subject an active ingredient comprising either human PSA, or an expression system capable of generating in situ said human PSA. Claim 5, which depends on claim 1, clearly recites wherein the active ingredient is formulated to be encapsulated in a liposome or coupled to a liposome and wherein said liposomes optionally contain an adjuvant. Claim 6 also recites the method of claim 1 which further includes at least one adjuvant capable enhancing said antitumor immune response. Claim 7, which depends on claim 6, recites a list of adjuvants which include monophosphoryl lipid A. Since the claims, and in particular, claims 6 and 7, clearly recite the combination of **either** a protein PSA antigen or an expression system capable of generating in situ said PSA and an adjuvant such as monophosphoryl lipid A, there can be no doubt that Spitler et al. contemplated applicant's claimed combination of nucleic acid encoding an antigen and non-DNA adjuvant in the context of liposome administration. If Spitler had intended the adjuvant to be only administered with the protein form of PSA, then claim 6 would have included a limitation that indicated that the adjuvant would only be administered with the protein form of the antigen. However, claim 6 clearly reads on the administration of the adjuvant with **either** the protein or the nucleic acid form of the PSA antigen. The applicant is reminded that 35 U.S.C. 282 states that each claim, whether independent or dependant, of an issued U.S. Patent is presumed valid.

Further, regarding the teachings of the Spitler specification, the teachings of column 8, lines 9-12, clearly states that as an embodiment of the instant invention recombinant vectors included in a liposome injectable "as described above" can be administered to the subject. The description of liposome injectables referenced in column 8, lines 9-12, can be found in column 7 which clearly teaches that liposomes may also include immune system adjuvants such as lipid A. Regarding intracellular delivery, please note that at the time of filing, the skilled artisan was well versed in the delivery of DNA to cells using liposomes and was likewise well versed in the use of liposomes to deliver adjuvants. Liposomes, depending on their composition, are fully capable of slow release of their contents to the extracellular space and are also fully capable of introducing their contents directly into a cell. Thus, it is clear from both the teachings of the specification and the claims of the 5,925,362 patent, that Spitler et al. teaches all the elements of the applicant's invention. As such, Spitler et al. anticipates the invention as claimed.

In conclusion, the office finds that the claims of the Spitler patent teach each and every element of the claims as required by U.S.C. 102 and that the specification of the Spitler patent supports the subject matter of the Spitler claims. The office also reiterates that 35 U.S.C. 282 states that each claim, whether independent or dependant, of an issued U.S. Patent is presumed valid.

***Claim Rejections - 35 USC § 103***

The rejection of previously pending claims 1, 3-5, 17-25, 29-34, 36-38, 40, 42, 44-45 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,925,362, hereafter referred

to as Spitler et al., in view of Fynan et al., Golding et al., and Sedegah et al. is withdrawn over the canceled claims, and maintained over new claims 66-68.

The applicant argues that this grounds of rejection should not be applied to the new claims because Spitler et al. does not teach the intracellular delivery of non-DNA adjuvant. This argument has been addressed in detail above and has not been found persuasive as Spitler et al. claims and teaches the delivery of liposomes comprising nucleic acid encoding a tumor antigen and a non-DNA adjuvant such as MPL.

The applicant further argues that both Fynan et al. and Sedegah et al. are silent in regards to adjuvant administration and that Golding et al. teaches extracellular use of non-DNA adjuvant. The applicant also argues that the hypothesized adjuvant mechanisms as of the priority date assumed extracellular function, such that the skilled artisan would not have been motivated to try and deliver the adjuvant intracellularly. In response, the claims of the Spitler patent set forth the administration of the nucleic acid and the non-DNA adjuvant in a form, i.e. encapsulated by liposomes, that results in intracellular delivery. As such, the motivation of intracellular delivery of the non-DNA adjuvant is provided by Spitler et al.

Further, it is noted that Spitler et al. only differs from the instant claims 66-68, which recite that the antigen of interest is a viral antigen from HA, HBV, or HIV, or a circumsporozoite antigen from a malarial parasite, in the nature of the antigen administered. Spitler et al. teaches a tumor antigen, rather than a viral or parasite antigen. Fynan et al. and Sedegah et al. were cited for providing the teachings and motivation to generate immune responses against these antigens by administering DNA encoding the antigen. The applicant has not provided arguments

traversing the teachings of Fynan et al. and Sedegah et al. for their teachings to administer viral or parasite antigens.

Therefore, the rejection of record is maintained over new claims 66-68.

It is noted that this grounds of rejection has not been applied to new claims 48-59, 63-64, and 74-75 for the following reasons: while new claims 60-62, 65, and 69-73 are anticipated by the claims and teachings of Spitler et al., see above, remaining new claims 48-59, 63-64, and 74-75 are limited to core carrier particles coated with both the nucleic acid encoding the antigen and the non-DNA adjuvant. None of Fynan et al., Sedegah et al. nor Golding teach coating core carrier particles with non-DNA adjuvant and Spitler, while teaching the administration of liposomes comprising the non-DNA adjuvant and the nucleic acid encoding an antigen, does not provide motivation for coating a core carrier particle with the non-DNA adjuvant. Claims 48-59, 63-64, and 74-75 are therefore considered free of the prior art of record.

***Nucleotide and/or Amino Acid Sequences***

This application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, the specification, at least on pages 43,45-46, and 48, contains numerous sequence disclosures encompassed by the definitions for amino acid sequences set forth in 37 CFR 1.821 (a)(1) and (a)(2) which are not identified by SEQ ID NOS and for which no paper sequence

listing or CFR has been filed. Paper and CRF sequence listings are required as set forth in the Notice to Comply. It is further suggested that the applicant review the specification for any additional sequences not identified by SEQ ID NOS. Also note that compliance to 37 CFR 1.821-1.825 requires that the specification be amended to recite SEQ ID NOS. for each recitation of a sequence in the specification.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your

application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER